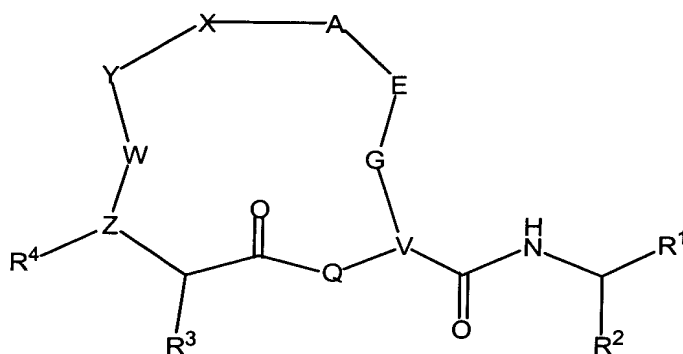


Amendments to the Claims:

The listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A macrocyclic compound, or enantiomers, stereoisomers, rotomers or tautomers of said compound, or pharmaceutically acceptable salts or solvates of said compound, said compound having the general structure shown in Formula I:



Formula I

wherein:

E, X and Y may be independently present or absent, and if present are independently selected from the moieties: alkyl, aryl, alkyl-aryl, heteroalkyl, heteroaryl, aryl-heteroaryl, alkyl-heteroaryl, cycloalkyl, alkyl ether, alkyl-aryl ether, aryl ether, alkyl amino, aryl amino, alkyl-aryl amino, alkyl sulfide, alkyl-aryl sulfide, aryl sulfide, alkyl sulfone, alkyl-aryl sulfone, aryl sulfone, alkyl-alkyl sulfoxide, alkyl-aryl sulfoxide, alkyl amide, alkyl-aryl amide, aryl amide, alkyl sulfonamide, alkyl-aryl sulfonamide, aryl sulfonamide, alkyl urea, alkyl-aryl urea, aryl urea, alkyl carbamate, alkyl-aryl carbamate, aryl carbamate, alkyl -hydrazide, alkyl-aryl hydrazide, alkyl hydroxamide, alkyl-aryl hydroxamide, alkyl sulfonyl, aryl sulfonyl, heteroalkyl sulfonyl, heteroaryl sulfonyl, alkyl carbonyl, aryl carbonyl, heteroalkyl carbonyl, heteroaryl carbonyl, alkoxy carbonyl, aryloxy carbonyl, heteroaryloxy carbonyl, alkylaminocarbonyl, arylaminocarbonyl, heteroarylaminocarbonyl or a combination thereof, with the proviso that E, X and Y may optionally be additionally substituted with moieties selected from the group consisting of aromatic, alkyl, alkyl-aryl, heteroalkyl, aryl-heteroaryl, alkyl-heteroaryl, cycloalkyl, alkyl ether, alkyl-aryl ether, alkyl sulfide, alkyl-aryl sulfide, alkyl sulfone, alkyl-aryl sulfone, alkyl amide, alkyl-aryl amide, alkyl sulfonamide, [[.]] alkyl amines, alkyl-aryl amines, alkyl-aryl sulfonamide,

alkyl urea, alkyl-aryl urea, alkyl carbamate, alkyl-aryl carbamate, halogen, hydroxylamino, alkyl carbazate, aryl carbazate;

$R^1 = \text{COR}^5$ or $\text{B}(\text{OR})_2$, wherein $R^5 = \text{H}, \text{OH}, \text{OR}^8, \text{NR}^9\text{R}^{10}, \text{CF}_3, \text{C}_2\text{F}_5, \text{C}_3\text{F}_7, \text{CF}_2\text{R}^6, \text{R}^6, \text{COR}^7$ wherein $R^7 = \text{H}, \text{OH}, \text{OR}^8, \text{CHR}^9\text{R}^{10}$, or NR^9R^{10} , wherein $\text{R}^6, \text{R}^8, \text{R}^9$ and R^{10} are independently selected from the group consisting of H, alkyl, aryl, heteroalkyl, heteroaryl, cycloalkyl, cycloalkyl, arylalkyl, heteroarylalkyl, $\text{CH}(\text{R}^{1'})\text{COOR}^{11}$, $\text{CH}(\text{R}^{1'})\text{CONR}^{12}\text{R}^{13}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{COO R}^{11}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{CONR}^{12}\text{R}^{13}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{R}'$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{CONHCH}(\text{R}^{3'})\text{COO R}^{11}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{CONHCH}(\text{R}^{3'})\text{CONR}^{12}\text{R}^{13}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{CONHCH}(\text{R}^{3'})\text{CONHCH}(\text{R}^{4'})\text{COO R}^{11}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{CONHCH}(\text{R}^{3'})\text{CONHCH}(\text{R}^{4'})\text{CONR}^{12}\text{R}^{13}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{CONHCH}(\text{R}^{3'})\text{CONHCH}(\text{R}^{4'})\text{CONHCH}(\text{R}^{5'})\text{COO R}^{11}$, $\text{CH}(\text{R}^{1'})\text{CONHCH}(\text{R}^{2'})\text{CONHCH}(\text{R}^{3'})\text{CONHCH}(\text{R}^{4'})\text{CONHCH}(\text{R}^{5'})\text{CONR}^{12}\text{R}^{13}$, wherein $\text{R}^{1'}, \text{R}^{2'}, \text{R}^{3'}, \text{R}^{4'}, \text{R}^{5'}, \text{R}^{11}, \text{R}^{12}, \text{R}^{13}$, and R' are independently selected from a group consisting of H, alkyl, aryl, heteroalkyl, heteroaryl, cycloalkyl, alkyl-aryl, alkyl-heteroaryl, aryl-alkyl and heteroaralkyl;

Z is selected from O, N, or CH;

W may be present or absent, and if W is present, W is selected from $\text{C}=\text{O}$, $\text{C}=\text{S}$, SO_2 or $\text{C}=\text{NR}$;

Q is $(\text{NR})_p$, O, S, CH_2 , CHR, CRR' or a double bond towards V;

A is O, CH_2 , $(\text{CHR})_p$, $(\text{CHR}-\text{CHR}')_p$, $(\text{CRR}')_p$, NR, S, SO_2 , $\text{C}=\text{O}$ or a bond;

G is $(\text{CH}_2)_p$, $(\text{CHR})_p$, $(\text{CRR}')_p$, NR, O, S, SO_2 , $\text{S}(\text{O})_2\text{NH}$, $\text{C}=\text{O}$, or a double bond towards E or V;

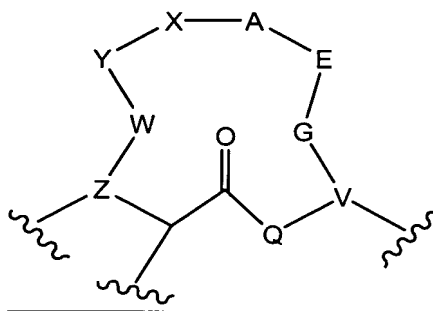
V is CH, CR or N;

R^2 is selected from the group consisting of H; C1-C10 alkyl; C2-C10 alkenyl; C3-C8 cycloalkyl; C3-C8 heterocycloalkyl, aryl, alkoxy, aryloxy, alkylthio, arylthio, amino, carbamate, urea, ketone, aldehyde, cyano, nitro; heteroaryl; alkyl-aryl; alkyl-heteroaryl; (cycloalkyl)alkyl and (heterocycloalkyl)alkyl, wherein said cycloalkyl is made of three to eight carbon atoms, and zero to six oxygen, nitrogen, sulfur, or phosphorus atoms, and said alkyl is of one to six carbon atoms;

p is a number from 0 to 6; and

R, R' , R^2 , R^3 and R^4 are independently selected from the group consisting of H; C1-C10 alkyl; C2-C10 alkenyl; C3-C8 cycloalkyl; C3-C8 heterocycloalkyl, aryl, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate,

urea, ketone, aldehyde, cyano, nitro; heteroaryl; alkyl-aryl; alkyl-heteroaryl; (cycloalkyl)alkyl and (heterocycloalkyl)alkyl, wherein said cycloalkyl is made of three to eight carbon atoms, and zero to six oxygen, nitrogen, sulfur, or phosphorus atoms, and said alkyl is of one to six carbon atoms; with said alkyl, heteroalkyl, alkenyl, heteroalkenyl, aryl, heteroaryl, cycloalkyl and heterocycloalkyl moieties may be optionally substituted, with said term "substituted" referring to optional and suitable substitution with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, heterocyclic, halogen, hydroxy, thio, alkoxy, aryloxy, alkylthio, arylthio, amino, amido, ester, carboxylic acid, carbamate, urea, ketone, aldehyde, cyano, nitro, sulfonamide, sulfoxide, sulfone, sulfonyl urea, hydrazide, hydroxamate and thiourea, with the proviso that the macrocycle ring represented by:



in Formula I represents at least a 11-membered macrocycle.

Claim 2 (currently amended): The compound of claim 1, wherein $R^1 = COR^5$, and R^5 is H, ΘH , $COOR^8$, or $CONR^9R^{10}$.

Claim 3 (original): The compound of claim 2, wherein $R^1 = COCONR^9R^{10}$, and is R^9 is H, R^{10} is H, $CH(R^1)COOR^{11}$, $CH(R^1)CONR^{12}R^{13}$, $CH(R^1)CONHCH(R^2)COOR^{11}$, $CH(R^1)CONHCH(R^2)CONR^{12}R^{13}$, or $CH(R^1)CONHCH(R^2)(R')$.

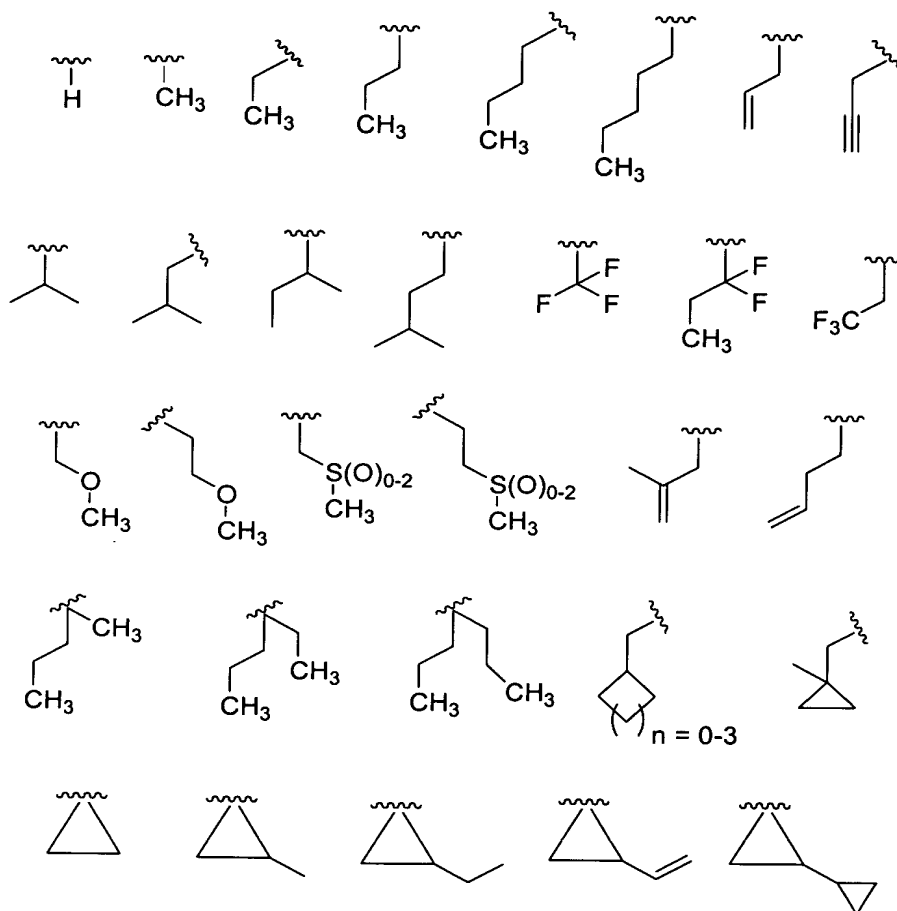
Claim 4 (currently amended): The compound of claim 3, wherein $R^{10} = CH(R^1)CONHCH(R^2)COOR^{11}$, $CH(R^1)CONHCH(R^2)CONR^{12}R^{13}$, or $CH(R^1)CONHCH(R^2)(R')$, wherein R^1 is H or alkyl, and R^2 is selected from the group consisting of phenyl, substituted phenyl, hetero atom-substituted phenyl, thiophenyl, cyclohexyl, cyclopentyl, cyclopropyl, piperidyl, pyridyl and 2-indanyl.

Claim 5 (original): The compound of claim 4, wherein R^1 is H.

Claim 6 (original): The compound of claim 5, wherein $R^2 =$ phenyl, thiophenyl, cyclohexyl, 2-indanyl, cyclopentyl, pyridyl, phenyl(4-HNSO₂NH₂), R^{11} is H or *tert*-butyl, R^{12} and R^{13} are methyl, and R' is hydroxymethyl or *tert*-butoxymethyl.

Claim 7 (original): The compound of claim 1, wherein R^2 is selected from the

group consisting of the following moieties:



Claim 8 (currently amended): The compound of claim 7 wherein R¹ = COR⁵, and R⁵ is H, OH, COOR⁸, or CONR⁹R¹⁰.

Claim 9 (original): The compound of claim 8 wherein V is CH.

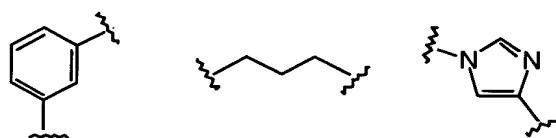
Claim 10 (original): The compound of claim 9 wherein Q is NR or O.

Claim 11 (original): The compound of claim 10 wherein G is CH₂.

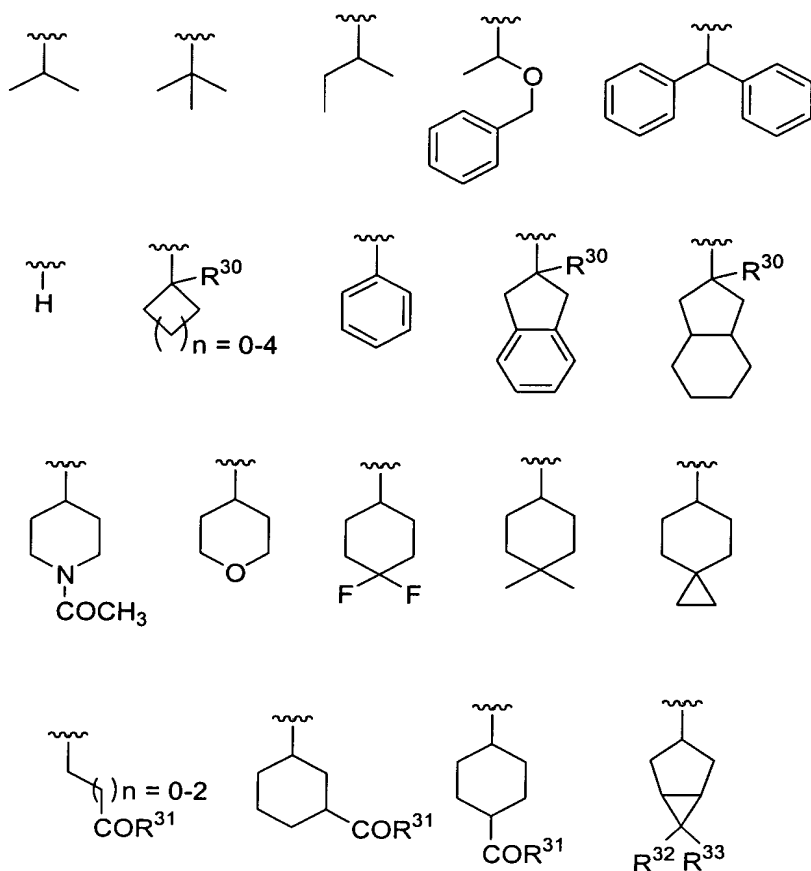
Claim 12 (original): The compound of claim 11 wherein A is O, NR, CH=CH or CH₂.

Claim 13 (original): The compound of claim 12 wherein E is alkyl, aryl, heteroalkyl, heteroaryl, alkyl, aryl, or cycloalkyl.

Claim 14 (original): The compound of claim 13 wherein E is selected from the group consisting of the moieties:



Claim 15 (original): The compound of claim 14 wherein R³ is selected from the group consisting of the moieties:



wherein R^{30} = H, CH_3 or other alkyl groups;

R^{31} = OH, O-alkyl, NH_2 , N-alkyl; and

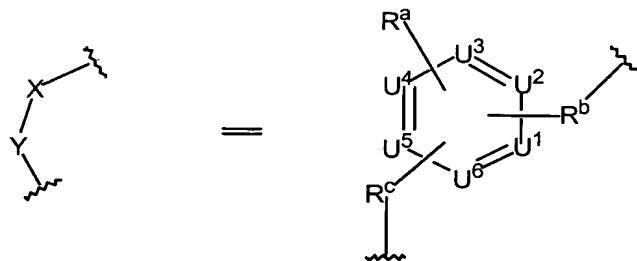
R^{32} and R^{33} may be the same or different and are selected independently from H, F, Cl, Br and CH_3 .

Claim 16 (original): The compound of claim 15 wherein $Z = \text{N}$ and $R^4 = \text{H}$.

Claim 17 (original): The compound of claim 16 wherein W is $\text{C}=\text{O}$.

Claim 18 (original): The compound of claim 17 wherein the moiety $X\text{-}Y$ is selected from the group consisting of: C1-C10 alkyl, alkyl, cycloalkyl, heteroalkyl, arylalkyl, aryl, heteroaryl and alkylaryl.

Claim 19 (original): The compound of claim 18, wherein:



wherein R^b is connected directly to A and R^c is connected directly to W; and the

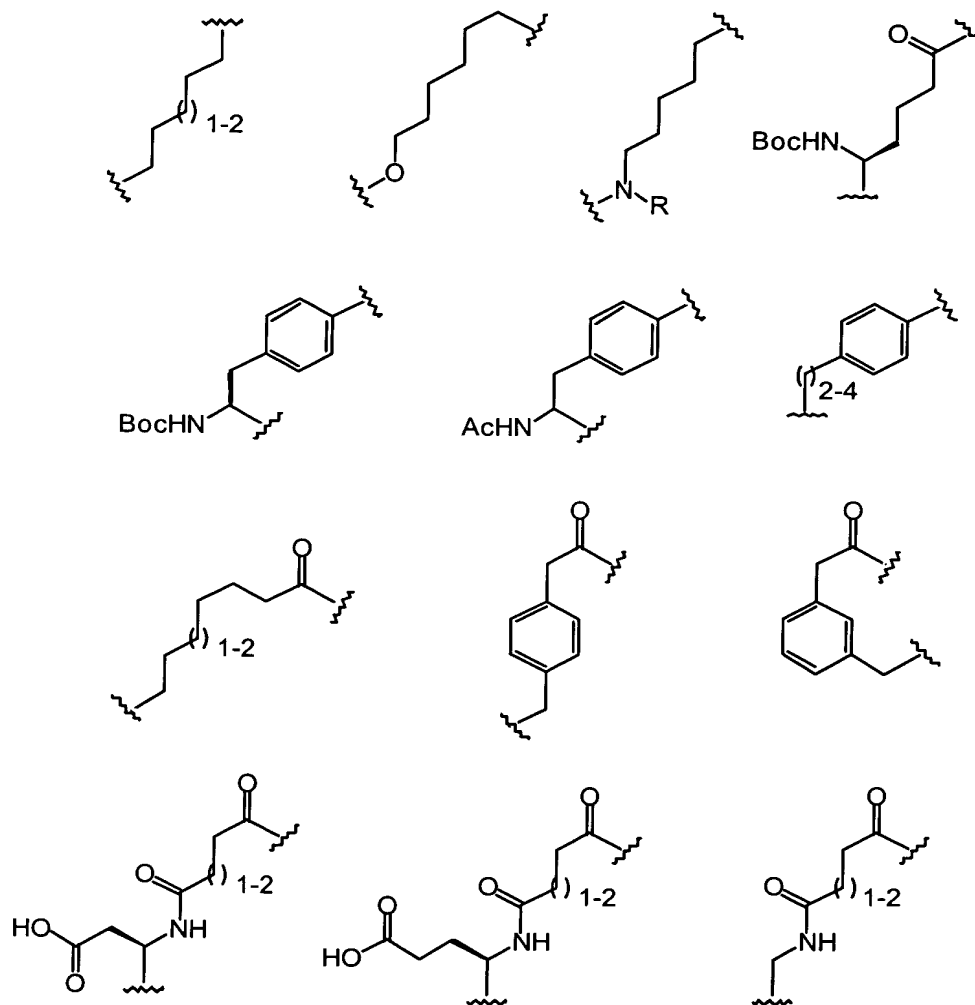
moiety U^1 , U^2 , U^3 , U^4 , U^5 and U^6 form either a six membered carbon ring, or a five or six membered ring with one or more heteroatoms;

R^a = H, alkyl, alkoxy, hydroxy, alkylthio, halogen, nitro, cyano, carboxylic acid, ester, amide, amino, nitrile, or CF_3 ;

R^b is a bond, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, O, S, SO_2 , NH, O(alkyl), S(alkyl), SO_2 (alkyl) or N(alkyl); and

R^c is a bond, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, O, S, SO_2 , NH, O(alkyl), S(alkyl), SO_2 (alkyl), N(alkyl) or CH_2 -N(alkyl) with the CH_2 being linked to the aromatic ring.

Claim 20 (original): The compound of claim 18 wherein the moiety X-Y is selected from the group consisting of the following structures:



Claim 21 (previously amended): A composition comprising as an active ingredient a compound of claim 1 and a pharmaceutically acceptable carrier.

Claim 22 (previously amended): The composition of claim 21 wherein said compound of claim 1 is present in amounts effective to inhibit hepatitis C nonstructural protein-3 protease (HCV NS3 protease).

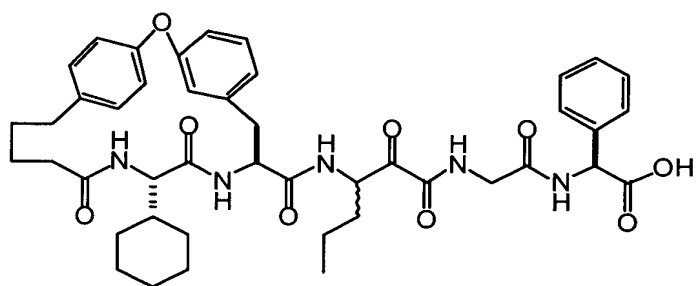
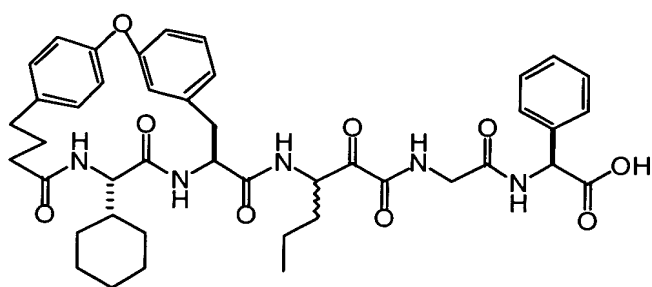
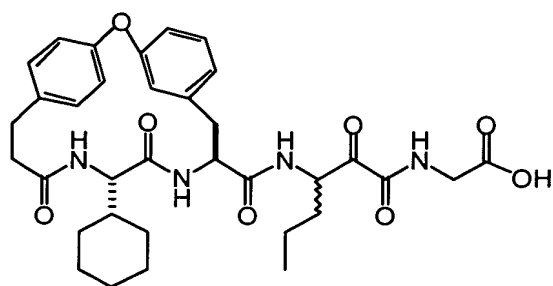
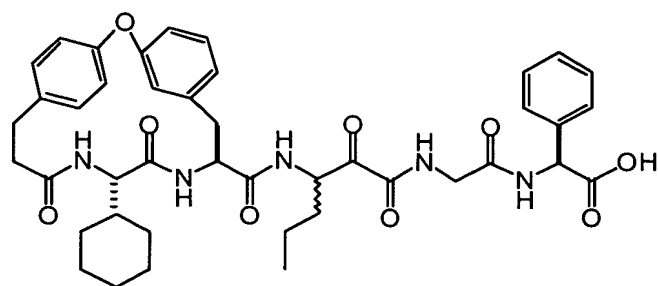
Claim 23 (previously canceled).

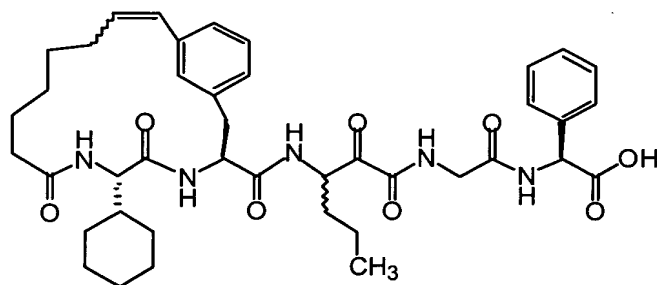
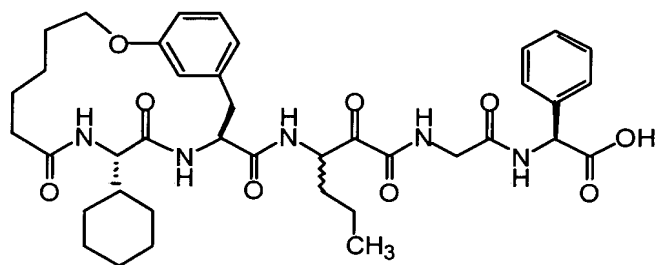
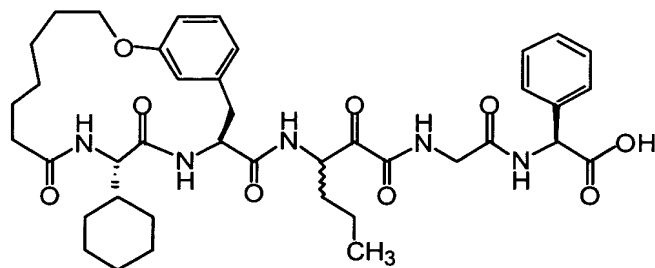
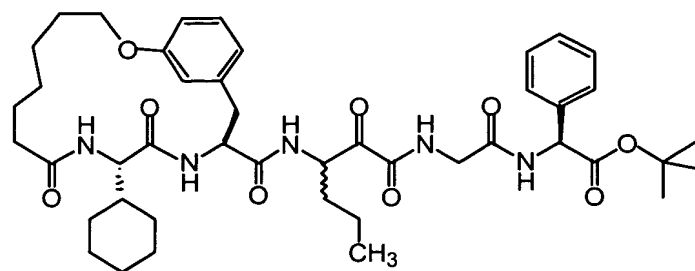
Claim 24 (withdrawn from consideration).

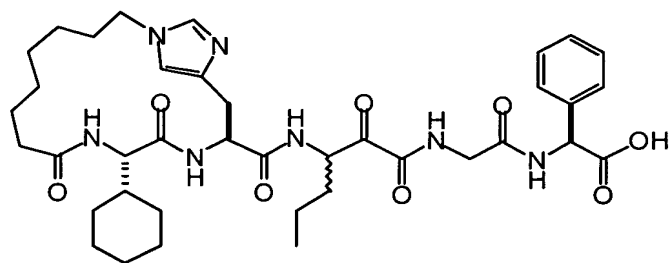
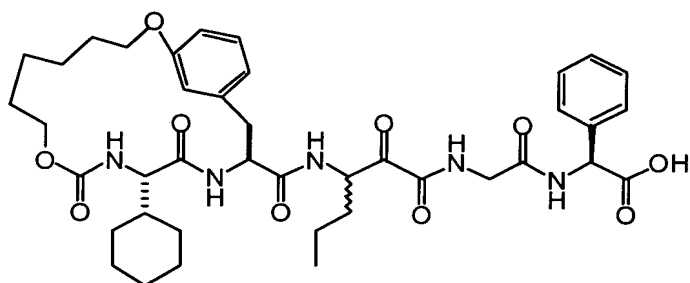
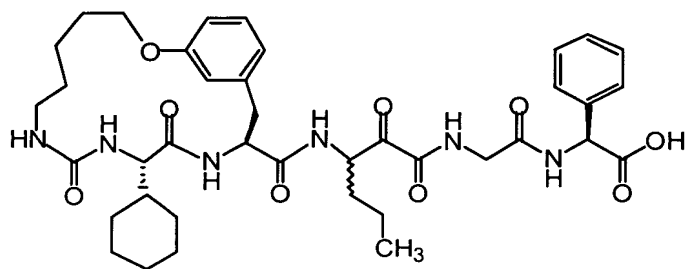
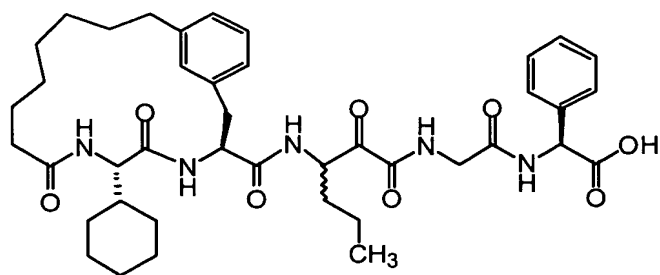
Claim 25 (withdrawn from consideration).

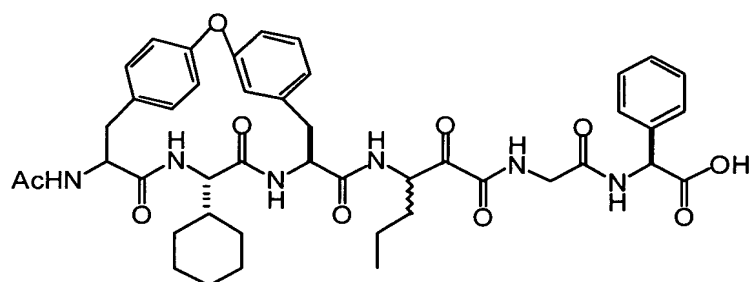
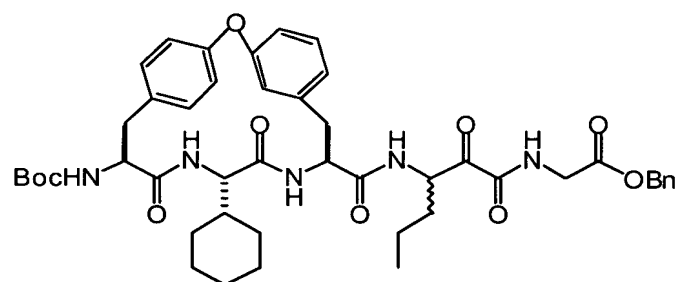
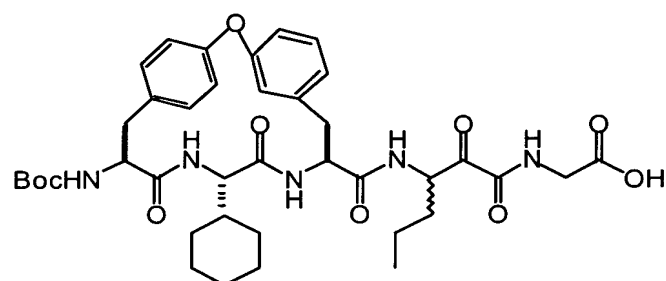
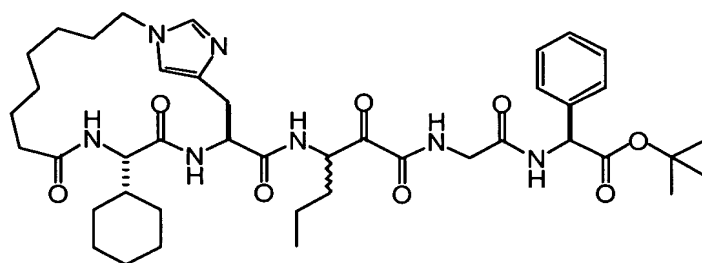
Claim 26 (previously amended): A method of preparing a composition for inhibiting hepatitis C nonstructural protein-3 protease (HCV NS3 protease), said method comprising bringing into intimate contact a compound of claim 1 in an amount effective to cause said inhibition and a pharmaceutically acceptable carrier.

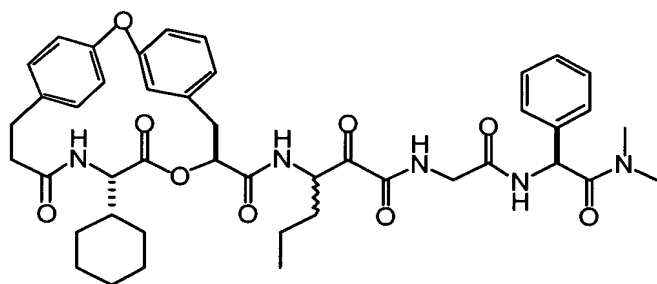
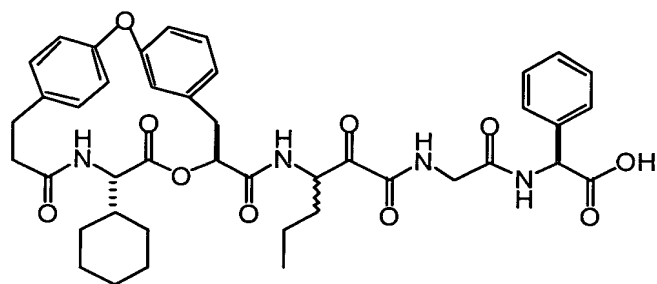
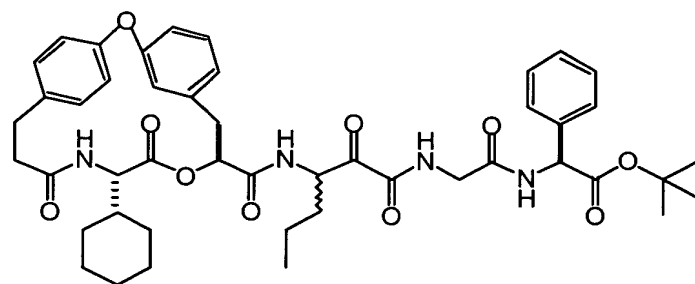
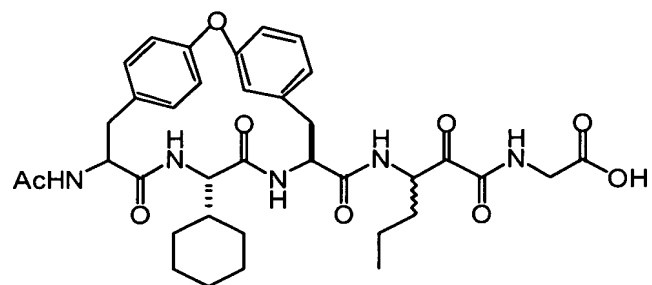
Claim 27 (previously amended): A compound exhibiting HCV NS3 protease inhibitory activity, or enantiomers, stereoisomers, rotamers or tautomers of said compound, or pharmaceutically acceptable salts or solvates of said compound, said compound being selected from the group of compounds with structures listed below:

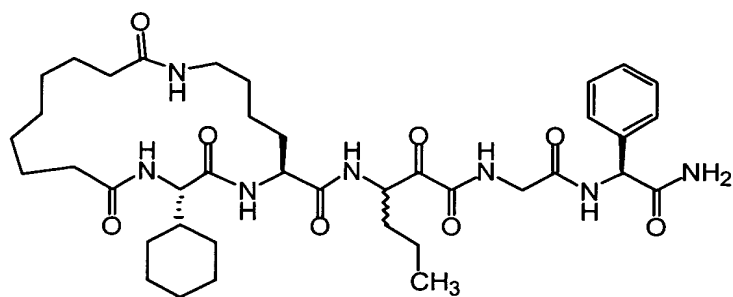
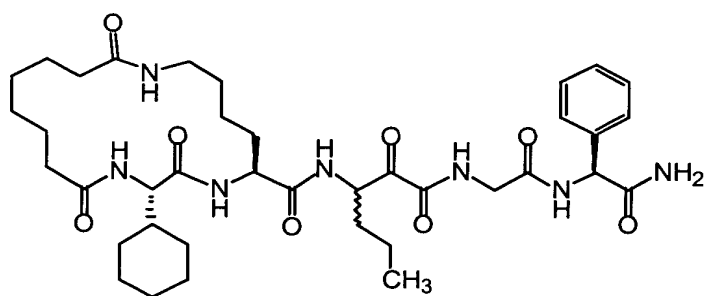
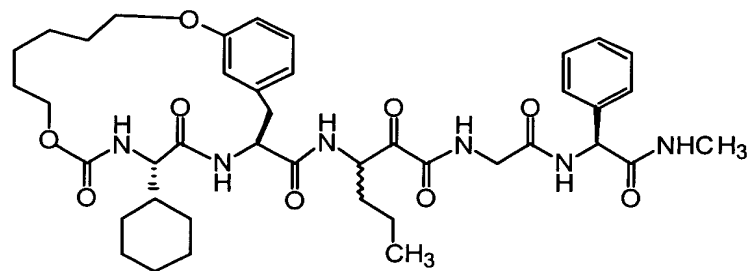
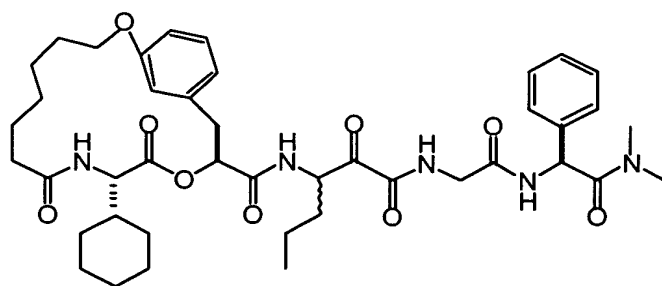


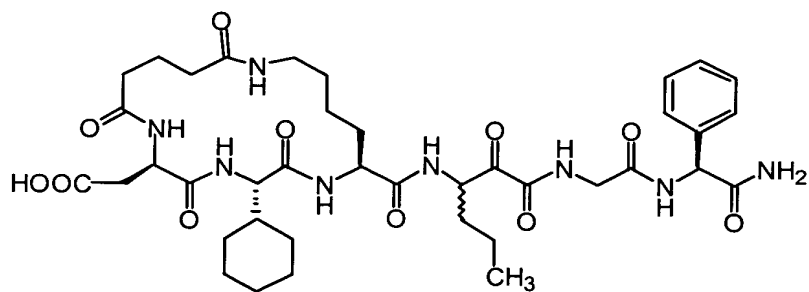
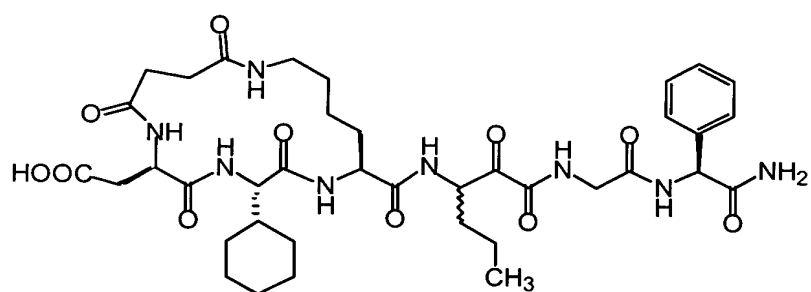
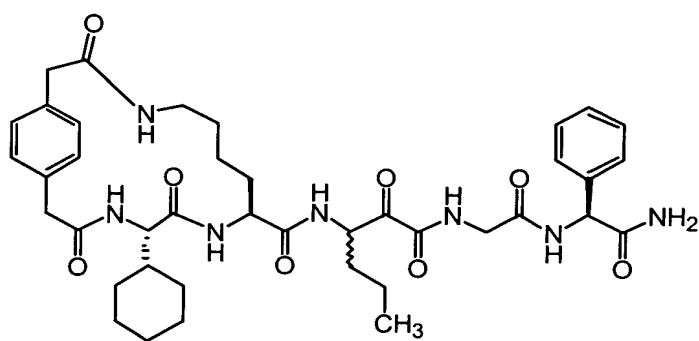
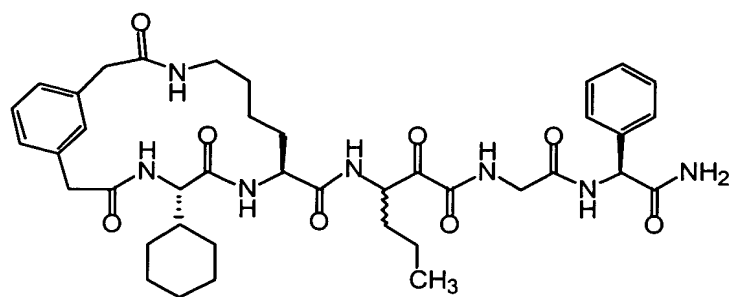


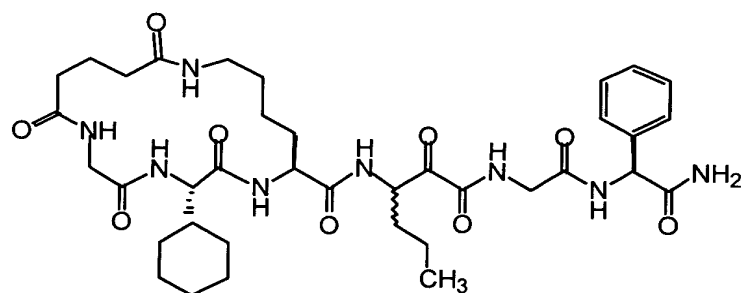
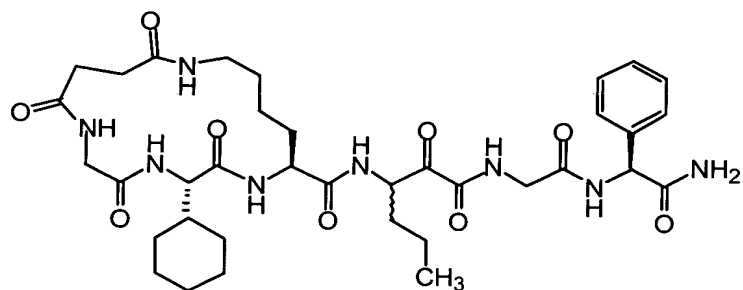
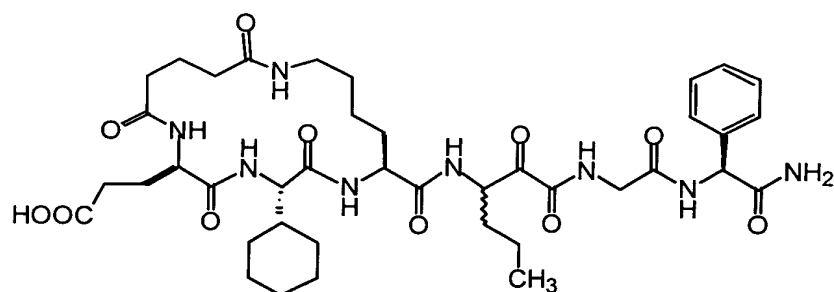
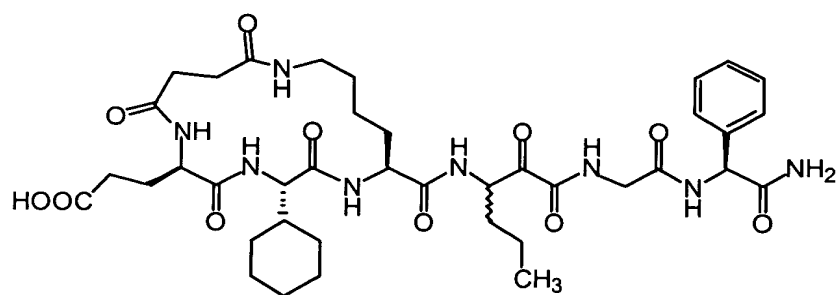












Claim 28 (currently amended): A composition for inhibiting hepatitis C nonstructural protein-3 protease (HCV NS3 protease), said composition comprising one or more compounds in claim 27 in amounts ~~therapeutically effective~~ to cause said inhibition and a pharmaceutically acceptable carrier.

Claim 29 (previously presented): The composition of claim 28, additionally

containing an antiviral agent.

Claim 30 (previously presented): The composition of claim 28 or claim 29, still additionally containing an interferon.

Claim 31 (previously presented): The composition of claim 30, wherein said antiviral agent is ribavirin and said interferon is α -interferon.

Claim 32 (previously presented): A method of inhibiting HCV NS3 protease comprising administering a compound of claim 1 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

Claim 33 (previously presented): A method of inhibiting HCV NS3 protease comprising administering a composition of claim 21 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

Claim 34 (previously presented): A method of inhibiting HCV NS3 protease comprising administering a compound of claim 27 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

Claim 35 (previously presented): A method of inhibiting HCV NS3 protease comprising administering a composition of claim 28 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

Claim 36 (previously presented): A method of inhibiting hepatitis C virus replication comprising administering a compound of claim 1 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

Claim 37 (previously presented): A method of inhibiting hepatitis C virus replication comprising administering a composition of claim 21 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

Claim 38 (previously presented): A method of inhibiting hepatitis C virus replication comprising administering a compound of claim 27 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.

Claim 39 (previously presented): A method of inhibiting hepatitis C virus replication comprising administering a composition of claim 28 to a patient in need thereof for a time and under conditions effective to inhibit HCV NS3 protease.